

REMARKS

Upon entry of this amendment, claims 1-10, 13-33, and 36-50 are pending in the instant application. Among them, claims 14, 16-29, and 37-42 are withdrawn from consideration as being drawn to non-elected inventions. Applicants will cancel these claims upon indication of allowable subject matter. Claims 1-10, 13, 15, 30-33, 36, 43, 44, and 45-50 are currently under consideration.

Applicants note that the IDS has been considered by the Examiner. Applicants also note that the RCE submission filed on February 5, 2003 has been entered.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Double Patenting

Claims 1-10, 13, 15, 30-33, 36, and 43-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Pat. No. 5,834,188. Without conceding the appropriateness of this rejection, Applicants will submit a terminal disclaimer, if necessary, to obviate this rejection upon indication of allowable subject matter.

Claim rejections under 35 U.S.C. 103(a)

Claims 1 and 13 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes *et al.* (U.S. Pat. No. 5,863,733) in view of Wobus *et al.* (Differentiation 48: 173-182, 1991).

The Office Action essentially reiterated the rejection in the previous Office Action. In the “Response to Argument” section, the Office Action asserts that the scope of the term “morphogen-mediated biological effect,” as defined by the specification is broad. The Office Action points to page 19, lines 9-10 of the instant specification, which allegedly defines “morphogen-mediated biological effect” as “[t]he effect can be any biological effect resulting from exposure to or contact with a morphogen.” Thus, the Office Action concludes that “the

claim is broadly permissive to any biological effect, including the chronotropic effect disclosed by Wobus,” even though the biological effect disclosed by Wobus is heart muscle cell contraction not known to be related to morphogens at all based on the cited prior art. Applicants respectfully traverse the rejection.

As stated in the response to the previous Office Action, Wobus essentially teaches that mouse ES cells can differentiate to heart muscle cells under certain *in vitro* culture conditions, and that such differentiated heart muscle cells have certain features (expressing certain cell surface receptors, capable of responding to certain cardioactive drugs, etc.). However, it is unclear how this *in vitro* culture system has anything to do with any morphogens. By truncating the alleged definition of “morphogen-mediated biological effect” from “any biological effect resulting from exposure to or contact with a morphogen” to “any biological effect,” the Office Action grossly misinterpreted the meaning of “morphogen-mediated biological effect,” which leads to the wrong conclusion that all elements necessary for a *prima facie* case of obviousness are present. This is analogous to saying that a person is liable for *any* credit card bill (including those of others), since he is liable for *any* credit card bill resulting from use of his credit card.

Thus Applicants reiterate that all elements for establishing a *prima facie* case of obviousness are not present. Applicants respectfully request reconsideration and withdrawal of the obviousness rejection on this ground.

Claims 1-3, 6, 9, 13, 30-33, 36, 43-50 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes *et al.* in view of Wobus *et al.* and further in view of Nadal-Ginard.

The Office Action also reiterated the rejection stated in the previous Office Action. However, this basis of rejection also relies on the misinterpretation of the definition of “morphogen-mediated biological effect.” Therefore, as argued above, Foulkes, Wobus, and Nadal-Ginard each teach quite different subject matter unrelated to “morphogen-mediated biological effect.” Even for the sake of argument, the combined teachings of all three references, even though containing certain individual elements of the claimed invention, still fail to arrive at the claimed invention in the absence of a showing that the biological effect is a “morphogen-mediated” one.

Thus Applicants reiterate that all elements for establishing a *prima facie* case of obviousness are not present. Reconsideration and withdrawal of this rejection on ground of 35 USC 103(a) is respectfully requested.

Claims 1,13, 36, 43, 45-47, and 49 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes *et al.* in view of Smart *et al.*

Specifically, the Office Action asserts that Foulkes does not provide a motivation to apply the disclosed screen method to morphogenesis or morphogen-mediated biological effect in order to identify compounds which induce such effects; while Smart teaches in column 2, lines 61-64 “a method of screening candidate compounds for the ability to modulate the effective local or systemic concentration or level of morphogenic protein in an organism.” (emphasis added)

Therefore, Smart actually teaches a method of screening for compounds that modulate the expression level of endogenous morphogens, rather than screening for compounds that are morphogen analogs which function like morphogens. The former method seeks a compound that stimulates the expression of morphogens in an organism, so that the compound *indirectly* functions like a morphogen, and the method depends on the ability of the organism / tissue to synthesize morphogen upon stimulation by the compound (the identified compound does not act like a morphogen itself). The latter method, presently claimed, seeks a compound that *directly* acts like a morphogen itself, and the method does not depend on the ability of the organism / tissue to synthesize morphogen upon stimulation. Compounds identified by the Smart method would not be compounds identified by the claimed invention, and vice versa. Thus, the mechanisms underlying these two methods are so different that one method does not render the other obvious. This is analogous to the following situation. If the claimed invention could be viewed as a method for identifying sugar substitute, such as saccharine (so that the taste bud on the tongue feels the same sweetness of sugar without getting the unwanted calories of sugar), the Smart method would be viewed as a method aimed at identifying a compound that stimulates the synthesis of sugar itself in the tongue so that the taste bud feels the sweetness of real sugar. Alternatively, if the claimed invention could be viewed as a method of identifying a fever reducing agent that substitutes for acetaminophen, then ibuprofen might be one of the compounds identified by the claimed invention, which itself does not have any structural

relationship with acetaminophen, but nevertheless has the same biological effect of reducing fever. On the other hand, the Smart method would be aimed at identifying a drug that stimulates the synthesis of acetaminophen itself by the patient's body so that the fever may be reduced. Thus these two approaches are fundamentally independent of one another, and one cannot render the other legally obvious. The concept of identifying morphogen analogs was never mentioned or hinted at in either Smart or Foulkes. Thus, even assuming for the sake of argument that a skilled artisan would be motivated to combine the two references, the artisan would still not arrive at the claimed invention of identifying compounds that themselves induce a morphogen-mediated biological effect. And it naturally follows that the skilled artisan would not have a reasonable expectation of success of arriving at the claimed invention.

Thus Applicants reiterate that all elements for establishing a *prima facie* case of obviousness are not present. Reconsideration and withdrawal of this rejection on ground of 35 USC 103(a) is respectfully requested.

Claims 1-3, 6, 9, 13, 36, 43-47, and 49 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes *et al.* in view of Smart *et al.*, further in view of Nadal-Ginard.

As argued above, since none of the three cited references teaches or suggests a method of identifying a morphogen analog that itself induces morphogen-mediated biological effect. All the above argument applies, and the combined references (even if there is motivation to combine) still fail to teach or suggest the claimed invention. And it naturally follows that the skilled artisan would not have a reasonable expectation of success of arriving at the claimed invention.

Thus Applicants reiterate that all elements for establishing a *prima facie* case of obviousness are not present. Reconsideration and withdrawal of this rejection on ground of 35 USC 103(a) is respectfully requested.

Claims 1, 13, 36, 43, and 45-50 are rejected under 35 U.S.C. 103(a), as being unpatentable over Foulkes *et al.* in view of Smart *et al.*, further in view of Ozkaynak.

As the Office Action admits, "Ozkaynak expressly teaches screening for candidate compounds which alter endogenous morphogen levels (see example 9, column 37-38)." As argued above, none of the three cited references teach or suggest a method of identifying a

morphogen analog that itself induces morphogen-mediated biological effect. All the above argument applies, and the combined references (even if there is motivation to combine) still fail to teach or suggest the claimed invention. And it naturally follows that the skilled artisan would not have a reasonable expectation of success of arriving at the claimed invention.

Thus Applicants reiterate that all elements for establishing a *prima facie* case of obviousness are not present. Reconsideration and withdrawal of this rejection under 35 USC 103(a) are respectfully requested.

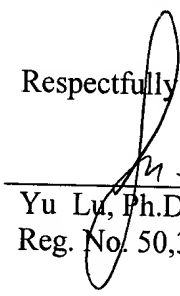
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,

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